10/685,870

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1201txs

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 18	Current-awareness alerts, saved answer sets, and current search transcripts to be affected by CERAB, COMPUAB, ELCOM, and SOLIDSTATE reloads
NEWS	6	NOV 30	PHAR reloaded with additional data
NEWS	7	DEC 01	LISA now available on STN
NEWS	8	DEC 09	12 databases to be removed from STN on December 31, 2004

NEWS EXPRESS	OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:48:41 ON 09 DEC 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:48:50 ON 09 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 8 DEC 2004 HIGHEST RN 795251-52-4
DICTIONARY FILE UPDATES: 8 DEC 2004 HIGHEST RN 795251-52-4

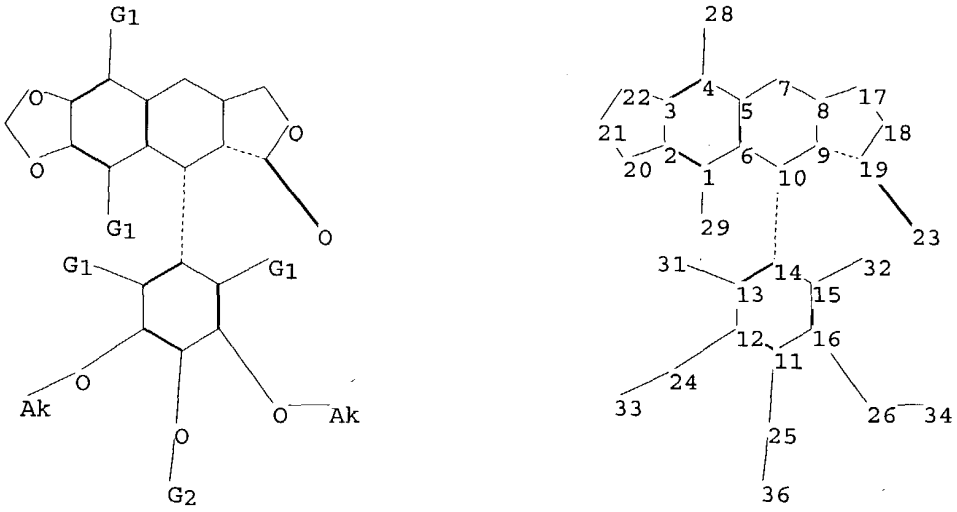
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10685870.str



chain nodes :
23 24 25 26 28 29 31 32 33 34 36
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
chain bonds :
1-29 4-28 10-14 11-25 12-24 13-31 15-32 16-26 19-23 24-33 25-36 26-34
ring bonds :
1-2 1-6 2-3 2-20 3-4 3-22 4-5 5-6 5-7 6-10 7-8 8-9 8-17 9-10 9-19
11-12 11-16 12-13 13-14 14-15 15-16 17-18 18-19 20-21 21-22
exact/norm bonds :
1-29 4-28 9-19 10-14 11-25 12-24 13-31 15-32 16-26 19-23 24-33 25-36
26-34
exact bonds :
2-20 3-22 5-7 6-10 7-8 8-9 8-17 9-10 17-18 18-19 20-21 21-22
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16
isolated ring systems :
containing 1 : 11 :

10/685,870

G1:H,Ak

G2:H,P

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:Atom 23:CLASS 24:CLASS 25:CLASS 26:CLASS 28:CLASS
29:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 36:CLASS

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 16:49:12 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 179 TO ITERATE

100.0% PROCESSED 179 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

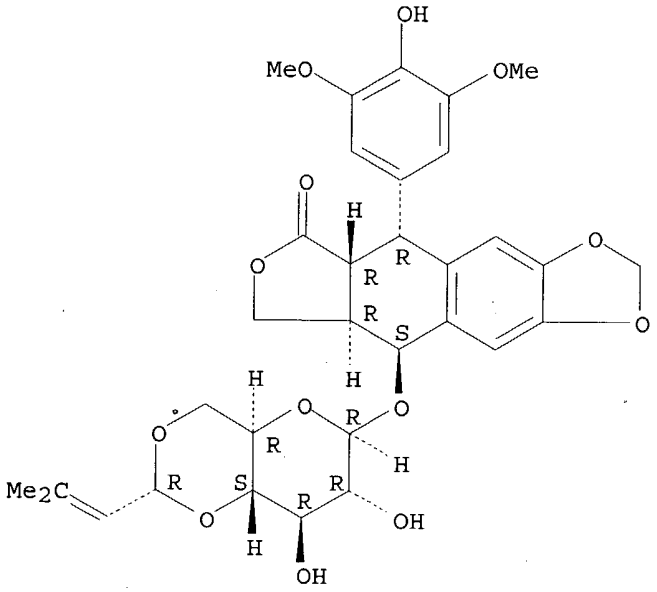
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2778 TO 4382
PROJECTED ANSWERS: 915 TO 1925

L2 50 SEA SSS SAM L1

=> d scan

L2 50 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[4,6-O-[(1R)-3-methyl-2-butenylidene]-β-D-glucopyranosyl]oxy]-, (5R,5aR,8aR,9S)- (9CI)
MF C32 H36 O13

Absolute stereochemistry.

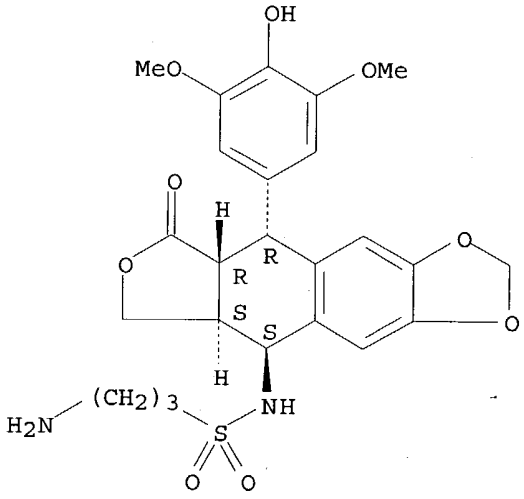


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2 50 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1-Propanesulfonamide, 3-amino-N-[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]- (9CI)
MF C24 H28 N2 O9 S

Absolute stereochemistry. Rotation (-).

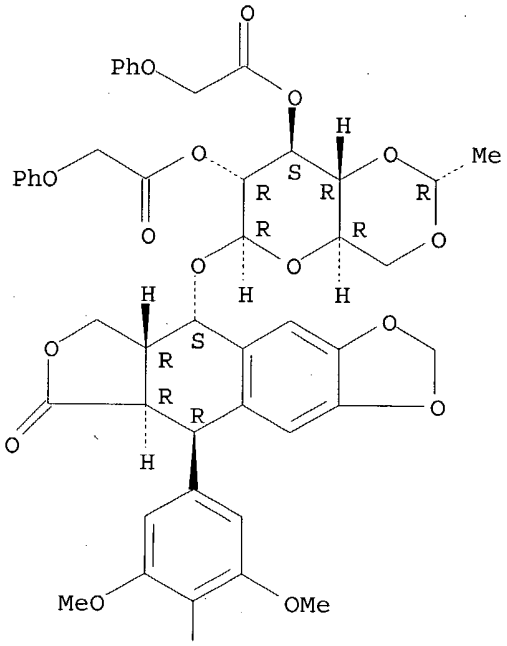


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

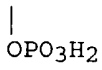
L2 50 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5-[3,5-dimethoxy-4-(phosphonooxy)phenyl]-9-[[4,6-O-ethylidene-2,3-bis-O-(phenoxyacetyl)-β-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-, [5R-[5α,5aβ,8aα,9β(R*)]]- (9CI)
MF C45 H45 O20 P
CI COM

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l1 ful
FULL SEARCH INITIATED 16:51:22 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 3667 TO ITERATE

100.0% PROCESSED 3667 ITERATIONS 1531 ANSWERS
SEARCH TIME: 00.00.01

```
L3          1531 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   157.10     157.31

FILE 'CAPLUS' ENTERED AT 16:51:33 ON 09 DEC 2004
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```
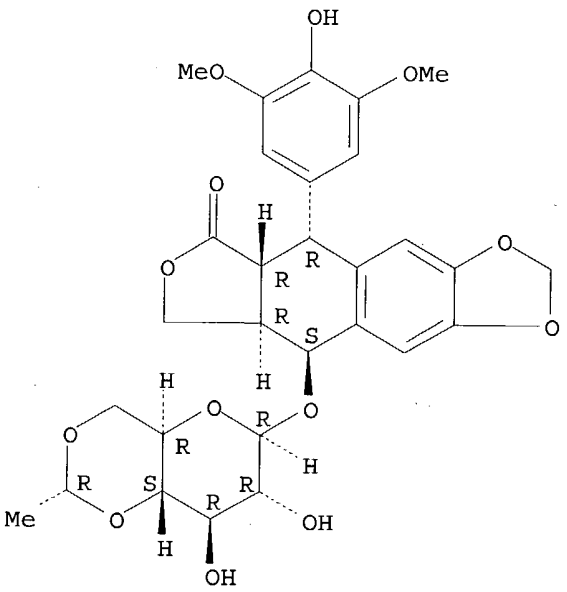



```
FILE COVERS 1907 - 9 Dec 2004  VOL 141 ISS 24
FILE LAST UPDATED: 8 Dec 2004  (20041208/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4          7295 L3

=> s l4 and podophyllotoxin
            1608 PODOPHYLLOTOXIN
              76 PODOPHYLLOTOXINS
            1623 PODOPHYLLOTOXIN
                   (PODOPHYLLOTOXIN OR PODOPHYLLOTOXINS)
L5           510 L4 AND PODOPHYLLOTOXIN

=> s l5 and cancer
          231350 CANCER
           33128 CANCERS
          240271 CANCER
                   (CANCER OR CANCERS)
L6           101 L5 AND CANCER

=> s l6 and tetracyclic
            4682 TETRACYCLIC
              13 TETRACYCLICS
            4692 TETRACYCLIC
                   (TETRACYCLIC OR TETRACYCLICS)
L7             0 L6 AND TETRACYCLIC

=> s l6 and mandrake plant
              41 MANDRAKE
          727184 PLANT
          404656 PLANTS
          900577 PLANT
                   (PLANT OR PLANTS)
```

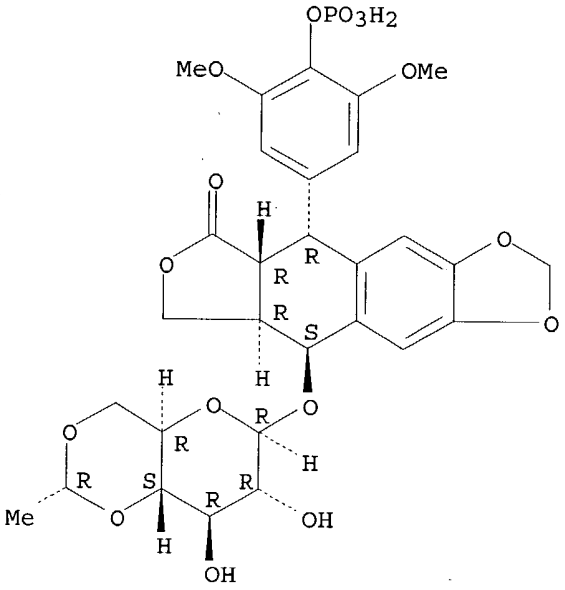
```
              0 MANDRAKE PLANT
                (MANDRAKE(W)PLANT)
L8            0 L6 AND MANDRAKE PLANT

=> s l6 and mandrake
             41 MANDRAKE
L9            1 L6 AND MANDRAKE

=> d l9 ibib hitstr abs

L9   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1997:79634  CAPLUS
DOCUMENT NUMBER:          126:112638
TITLE:                    Etoposide phosphate: what, why, where, and how?
AUTHOR(S):                Schacter, Lee
CORPORATE SOURCE:         Department of Medicine, Divison of Medical Oncology,
                          Yale Cancer Center, New Haven, CT, USA
SOURCE:                   Seminars in Oncology (1996), 23(6, Suppl. 13), 1-7
                          CODEN: SOLGAV; ISSN: 0093-7754
PUBLISHER:                Saunders
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
IT   33419-42-0, Etoposide 117091-64-2, Etoposide phosphate
     RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
     effector, except adverse); BPR (Biological process); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC
     (Process); USES (Uses)
        (etoposide and etoposide phosphate comparative pharmacokinetics and
        pharmacodynamics)
RN   33419-42-0  CAPLUS
CN   Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[[4,6-O-(1R)-
     ethylidene-β-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-5-(4-hydroxy-
     3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.  Rotation (-).
```




```
RN   117091-64-2  CAPLUS
```

CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5-[3,5-dimethoxy-4-(phosphonooxy)phenyl]-9-[[4,6-O-(1R)-ethylidene-β-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A review with 27 refs. The **podophyllotoxin** derivs. etoposide and teniposide are active in the treatment of a variety of malignant conditions. Both represent chemical modifications of podophyllin, an extract of Podophyllum peltatum (May apple, **mandrake**, Indian apple, wild lemon, or duck's foot), a plant long used as a folk remedy and recognized in the 19th century to be effective in the treatment of **cancer.** While etoposide is active in the treatment of many **cancers** and is widely used, it has a number of limitations due to its lack of water solubility Etoposide phosphate (Etopophos; Bristol-Myers Squibb Company, Princeton, NJ) is a water-soluble prodrug of etoposide that is rapidly and completely converted to the parent compound after i.v. dosing. The pharmacokinetic profile of etoposide after treatment with either etoposide or etoposide phosphate is identical. Toxicity and clin. activity also are the same. Because etoposide phosphate is water soluble and can be made up to a concentration of 20 mg/mL, however, it can be given as a 5-min bolus, in high doses in small vols., and as a continuous infusion. Furthermore, it is not formulated with polyethylene glycol, polysorbate 80 (Tween; ICI Americas, Wilmington, DE), and ethanol, and does not cause acidosis when given at high doses. The easier-to-use etoposide phosphate represents an improved formulation of etoposide.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION

FULL ESTIMATED COST	24.48	181.79

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.70	-0.70

FILE 'STNGUIDE' ENTERED AT 17:03:49 ON 09 DEC 2004
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 3, 2004 (20041203/UP).

=> s l6 and desoxypodophyl?
COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID
The query entered contains both search terms created by
structure-building or screen commands and text search terms. L#s
created via the STRUCTURE or SCREEN commands must be searched in the
structures files separately from text terms or profiles. The L#
answer sets from structure searches can be used in crossover searches
and can be combined with text terms.

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.02	182.81

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.70

FILE 'CAPLUS' ENTERED AT 17:14:17 ON 09 DEC 2004
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FILE COVERS 1907 - 9 Dec 2004 VOL 141 ISS 24
FILE LAST UPDATED: 8 Dec 2004 (20041208/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l6 and desoxypodophyl?
57 DESOXYPODOPHYL?
L10 3 L6 AND DESOXYPODOPHYL?

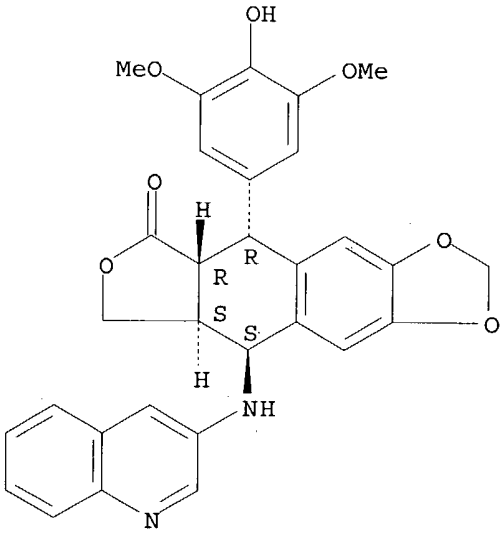
=> d l10 ibib hitstr abs 1-3

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:333694 CAPLUS
DOCUMENT NUMBER: 140:339123
TITLE: Preparation of **podophyllotoxin** derivatives as anticancer compounds
INVENTOR(S): Shi, Qian; Wang, Hui-kang; Oyama, Masayoshi; Vance, John Robert; Chen, Ming S.
PATENT ASSIGNEE(S): Plantaceutica Inc., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004033423	A2	20040422	WO 2003-US32547	20031014
WO 2004033423	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004138288	A1	20040715	US 2003-685870	20031014
PRIORITY APPLN. INFO.:			US 2002-417785P P	20021011

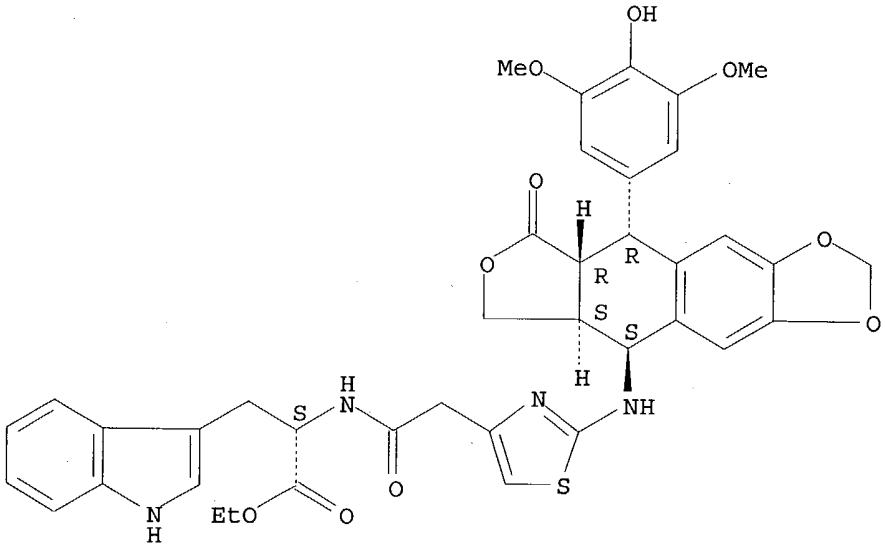
OTHER SOURCE(S): MARPAT 140:339123
IT **127882-77-3P 681138-02-3P 681138-04-5P**
681138-06-7P 681138-07-8P 681138-08-9P
681138-09-0P 681138-10-3P 681138-13-6P
681138-14-7P 681138-15-8P 681138-16-9P
681138-17-0P 681138-18-1P 681138-19-2P
681138-20-5P 681138-21-6P 681138-22-7P
681138-23-8P 681138-24-9P 681138-25-0P
681138-26-1P 681138-27-2P 681138-28-3P
681138-29-4P 681138-30-7P 681138-31-8P
681138-32-9P 681138-33-0P 681138-34-1P
681138-35-2P 681138-36-3P 681138-37-4P
681138-38-5P 681138-39-6P 681138-40-9P
681138-41-0P 681138-42-1P 681138-43-2P
681138-44-3P 681138-45-4P 681138-46-5P
681138-47-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **podophyllotoxin** derivs. as anticancer compds.)
RN 127882-77-3 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-(3-quinolinylamino)-, (5R,5aR,8aS,9S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



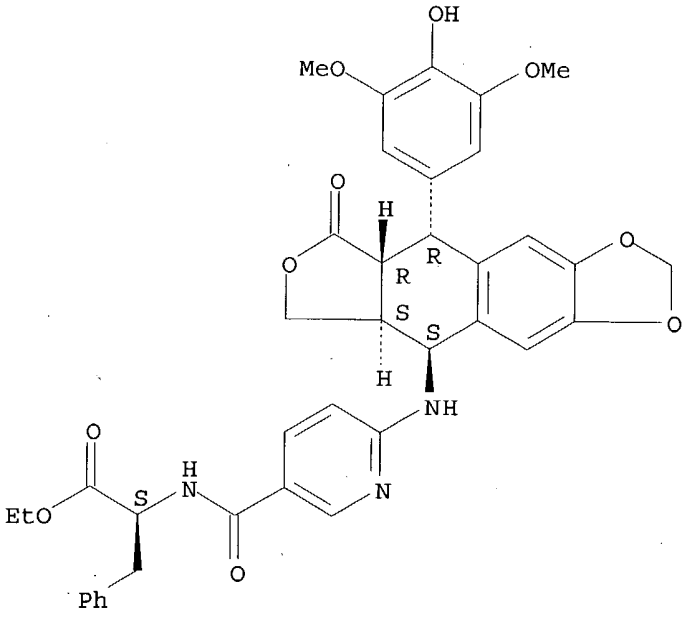
RN 681138-02-3 CAPLUS
CN L-Tryptophan, N-[[2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-4-thiazolyl]acetyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



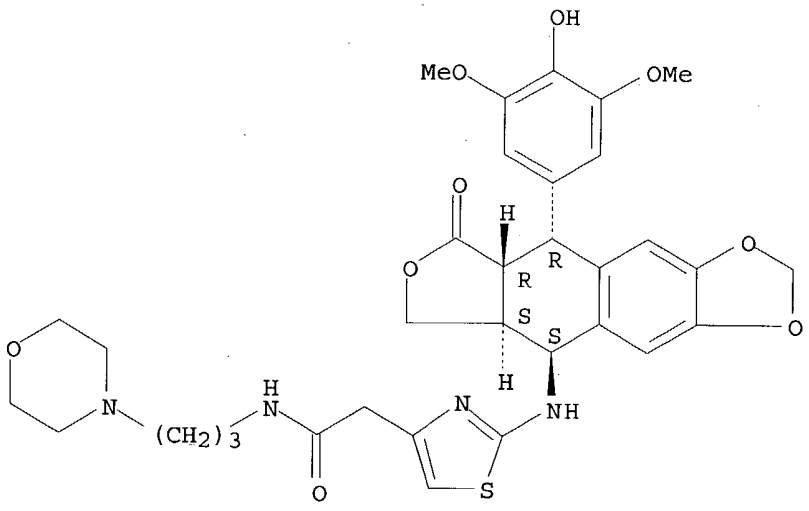
RN 681138-04-5 CAPLUS
CN L-Phenylalanine, N-[[6-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-3-pyridinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



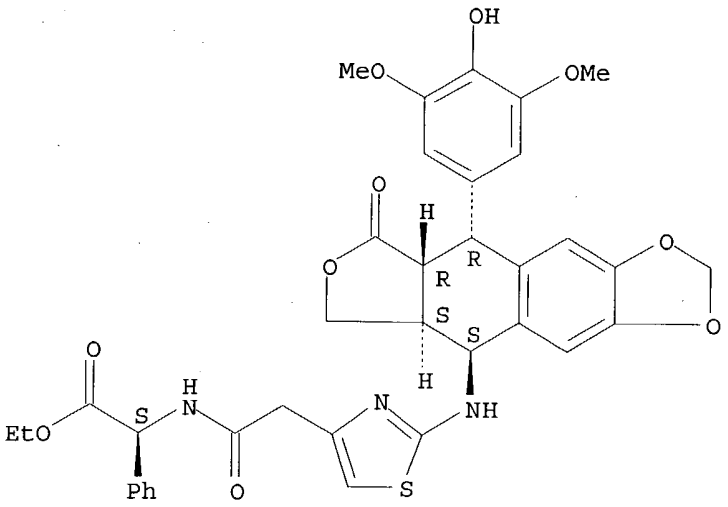
RN 681138-06-7 CAPLUS
CN 4-Thiazoleacetamide, 2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-N-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



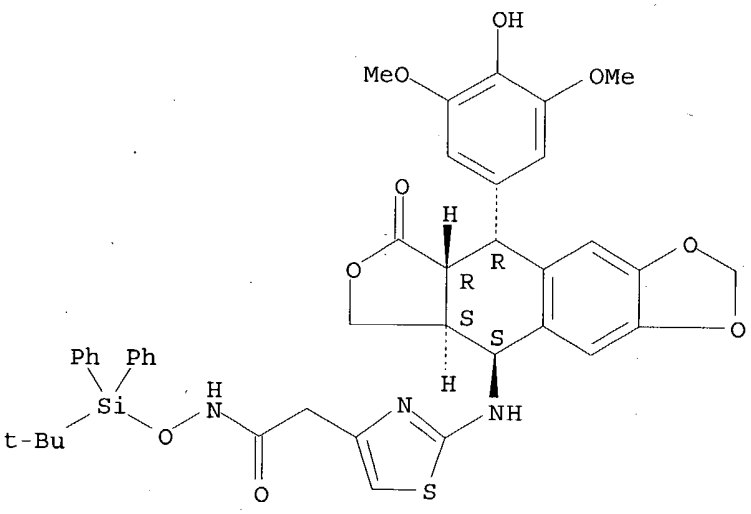
RN 681138-07-8 CAPLUS
CN Benzeneacetic acid, α-[[[2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-4-thiazolyl]acetyl]amino]-, ethyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



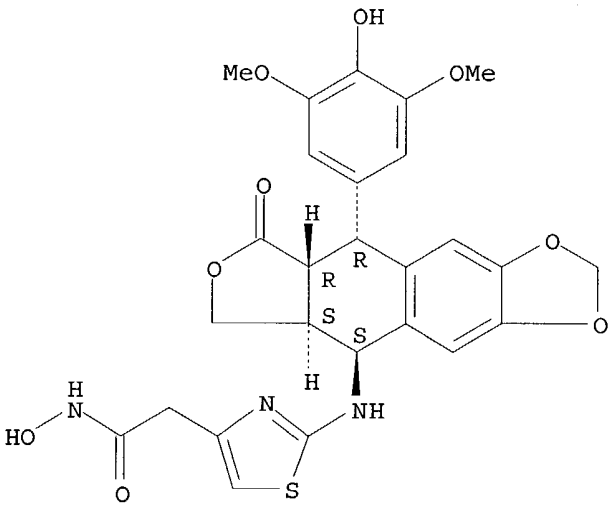
RN 681138-08-9 CAPLUS
CN 4-Thiazoleacetamide, N-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



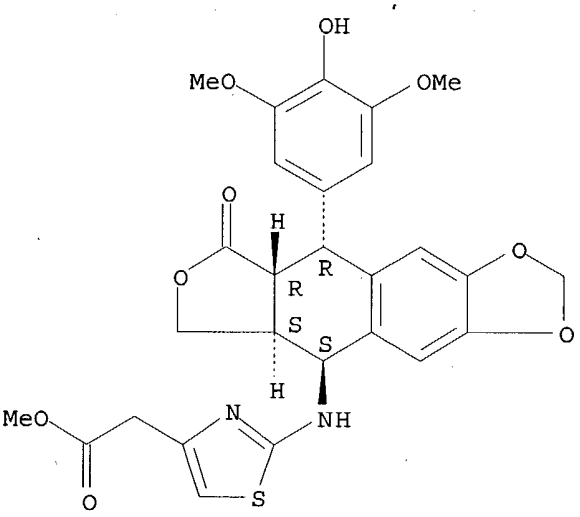
RN 681138-09-0 CAPLUS
CN 4-Thiazoleacetamide, 2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-N-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



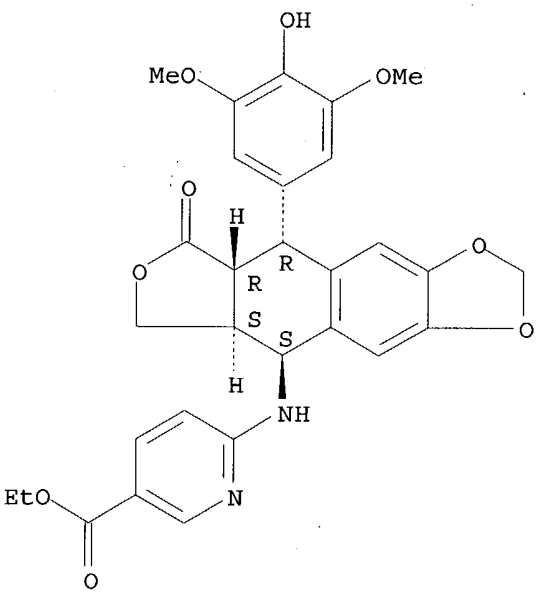
RN 681138-10-3 CAPLUS
CN 4-Thiazoleacetic acid, 2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



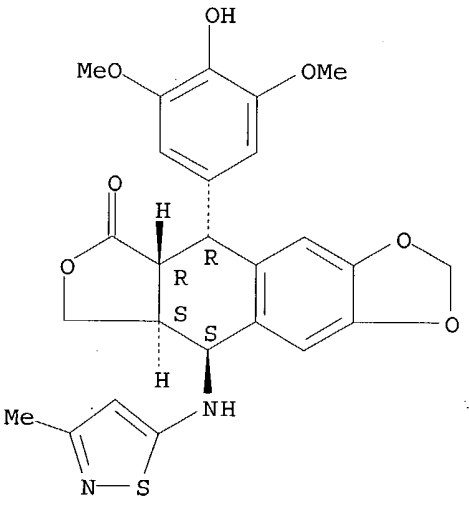
RN 681138-13-6 CAPLUS
CN 3-Pyridinecarboxylic acid, 6-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



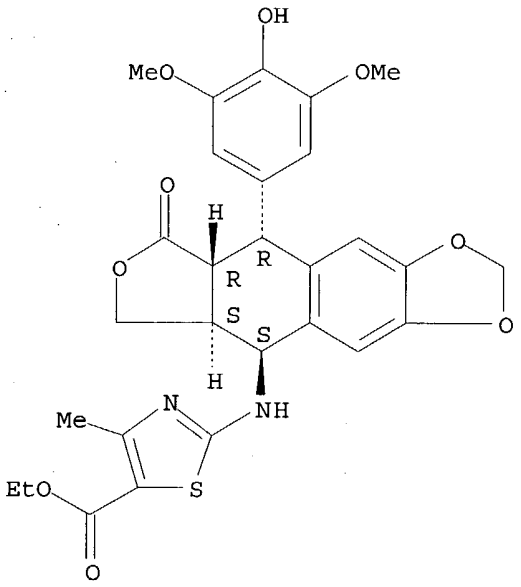
RN 681138-14-7 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(3-methyl-5-isothiazolyl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



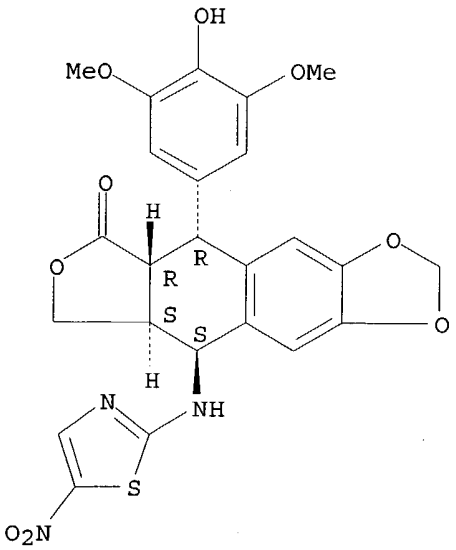
RN 681138-15-8 CAPLUS
CN 5-Thiazolecarboxylic acid, 2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



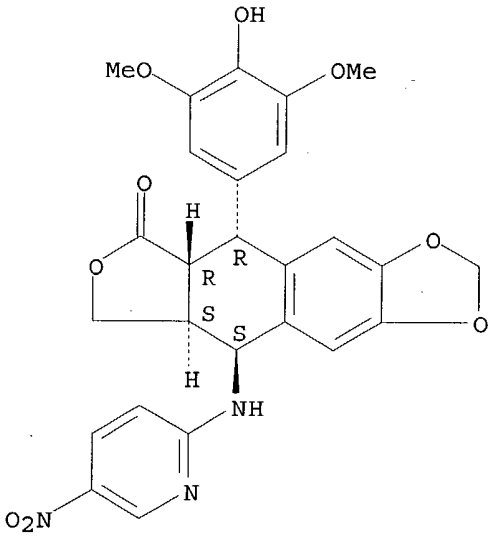
RN 681138-16-9 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(5-nitro-2-thiazolyl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



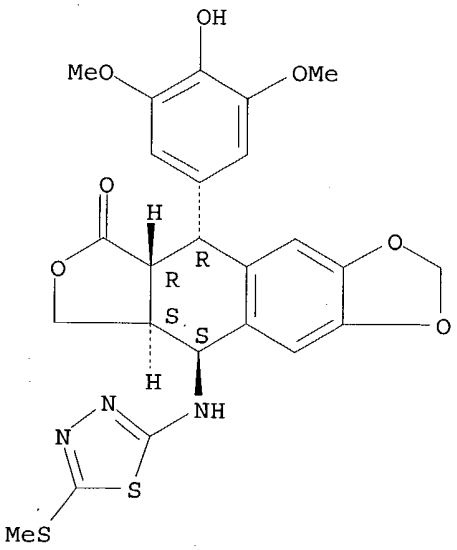
RN 681138-17-0 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(5-nitro-2-pyridinyl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



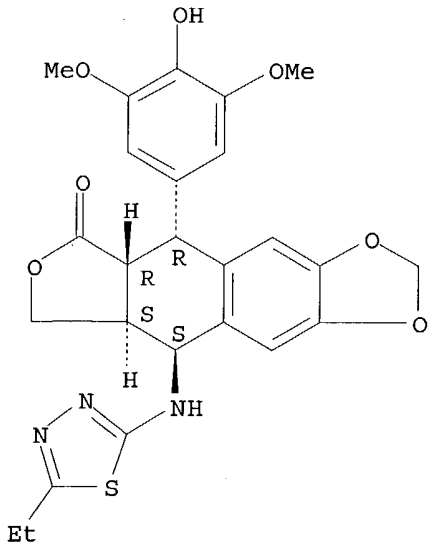
RN 681138-18-1 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[5-(methylthio)-1,3,4-thiadiazol-2-yl]amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



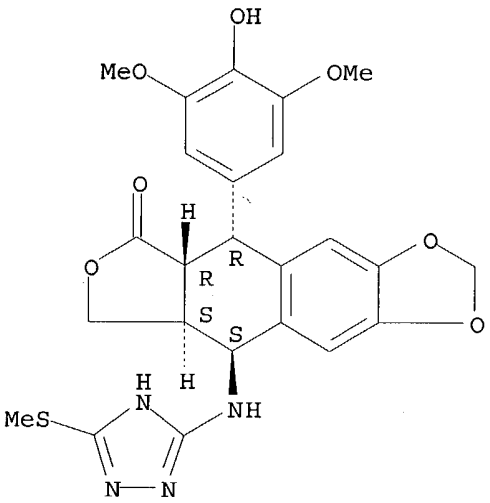
RN 681138-19-2 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



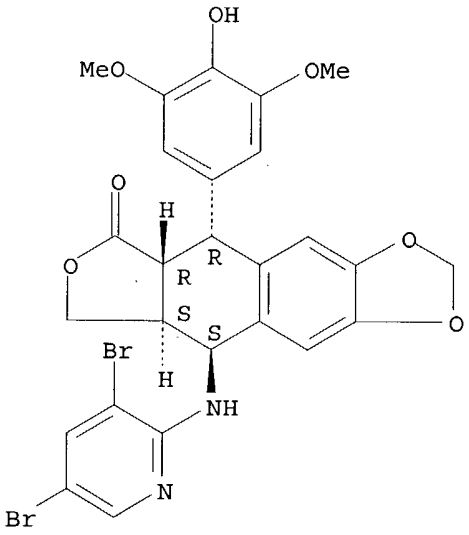
RN 681138-20-5 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[5-(methylthio)-1H-1,2,4-triazol-3-yl]amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



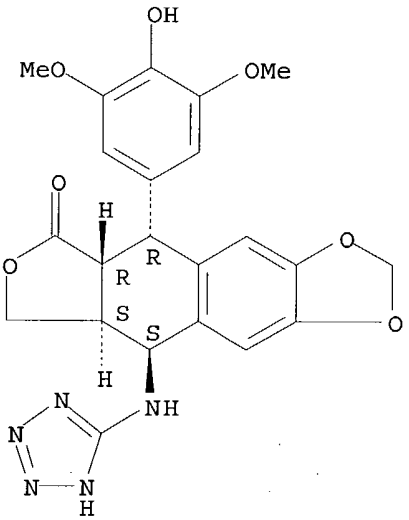
RN 681138-21-6 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[(3,5-dibromo-2-pyridinyl)amino]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



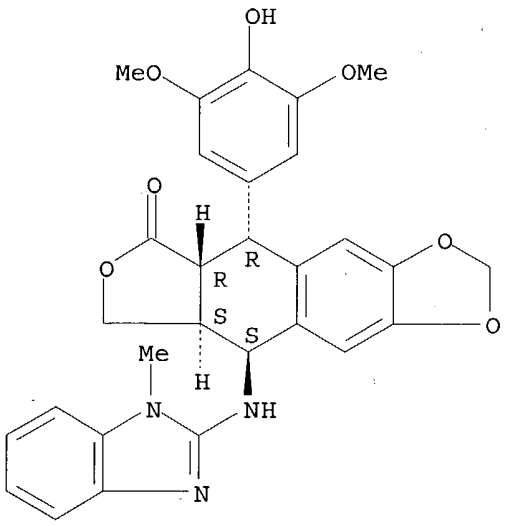
RN 681138-22-7 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-(1H-tetrazol-5-ylamino)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



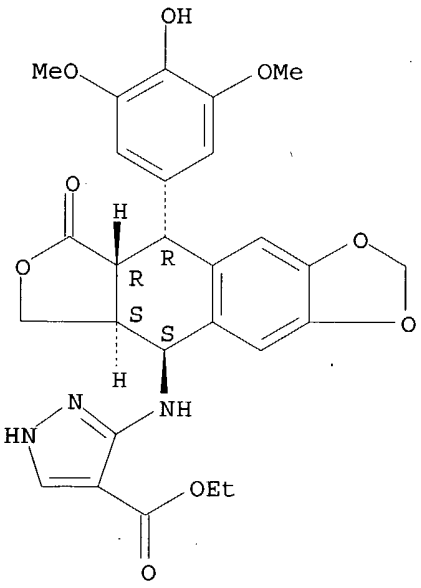
RN 681138-23-8 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(1-methyl-1H-benzimidazol-2-yl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



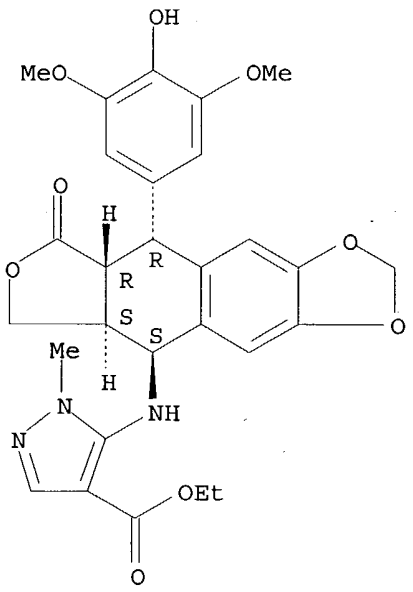
RN 681138-24-9 CAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 3-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



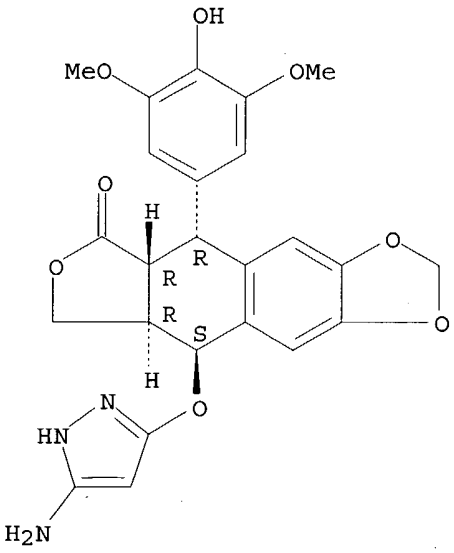
RN 681138-25-0 CAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-1-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



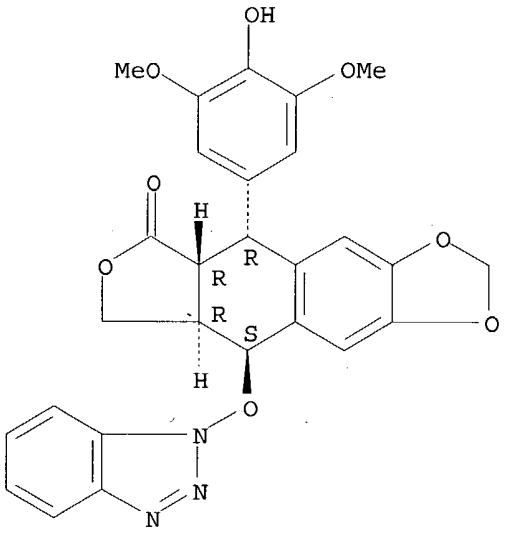
RN 681138-26-1 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[(5-amino-1H-pyrazol-3-yl)oxy]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



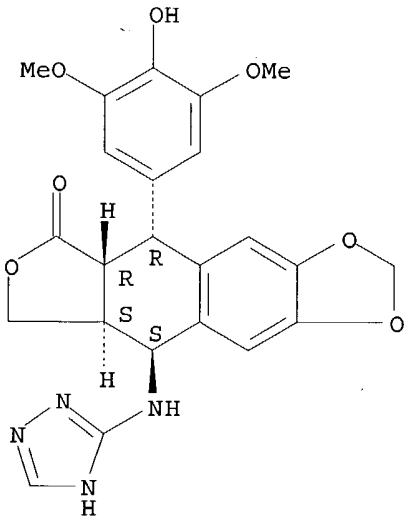
RN 681138-27-2 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-(1H-benzotriazol-1-yloxy)-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



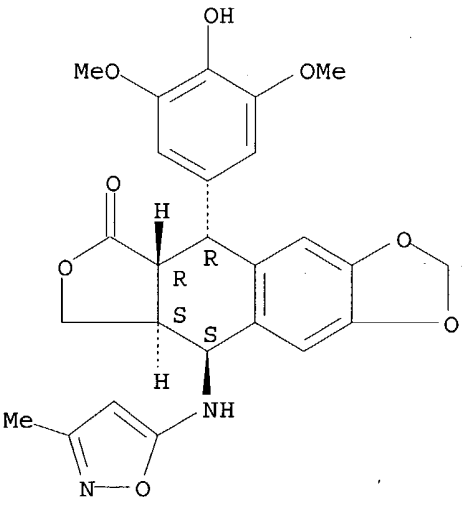
RN 681138-28-3 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-(1H-1,2,4-triazol-3-ylamino)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



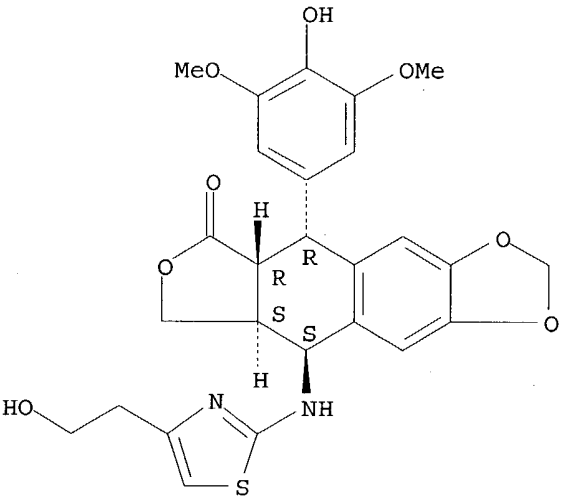
RN 681138-29-4 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(3-methyl-5-isoxazolyl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



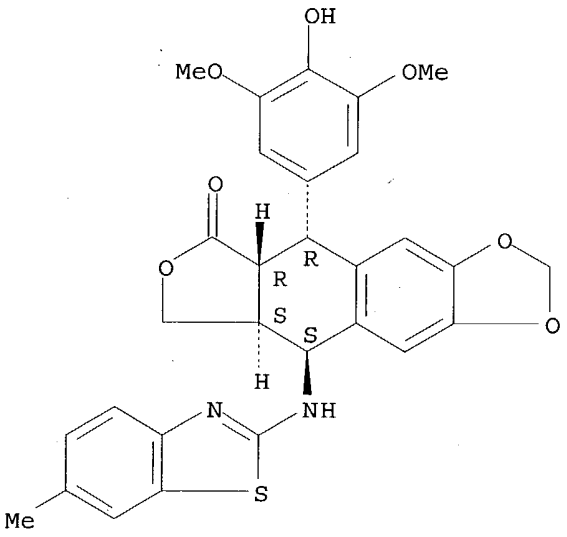
RN 681138-30-7 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[4-(2-hydroxyethyl)-2-thiazolyl]amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



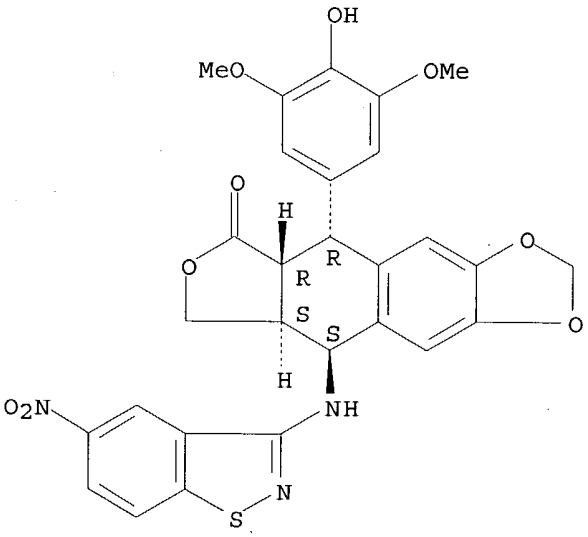
RN 681138-31-8 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(6-methyl-2-benzothiazolyl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



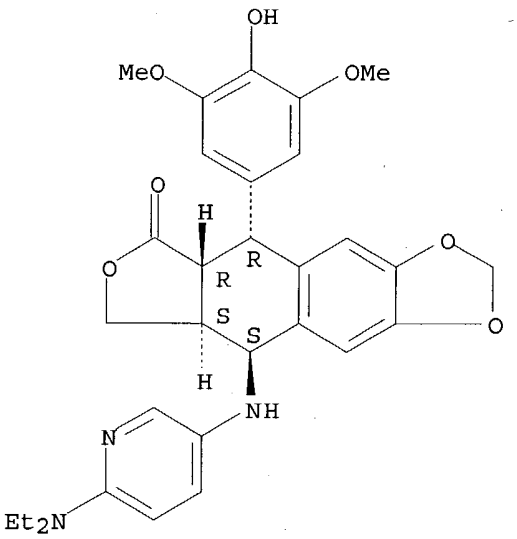
RN 681138-32-9 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(5-nitro-1,2-benzisothiazol-3-yl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



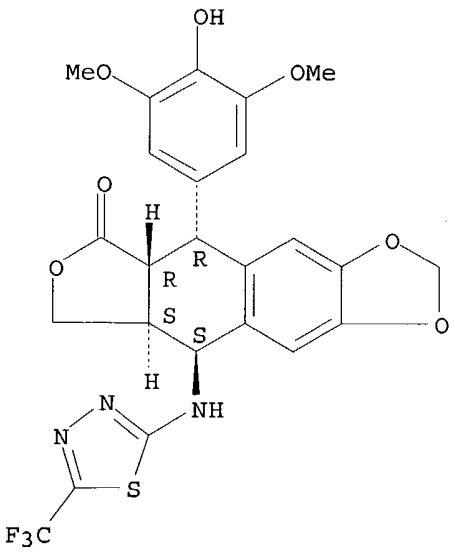
RN 681138-33-0 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[[6-(diethylamino)-3-pyridinyl]amino]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 681138-34-1 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 681138-35-2 CAPLUS
CN 3-Pyridinecarboxamide, N-(2-chloro-4-pyridinyl)-6-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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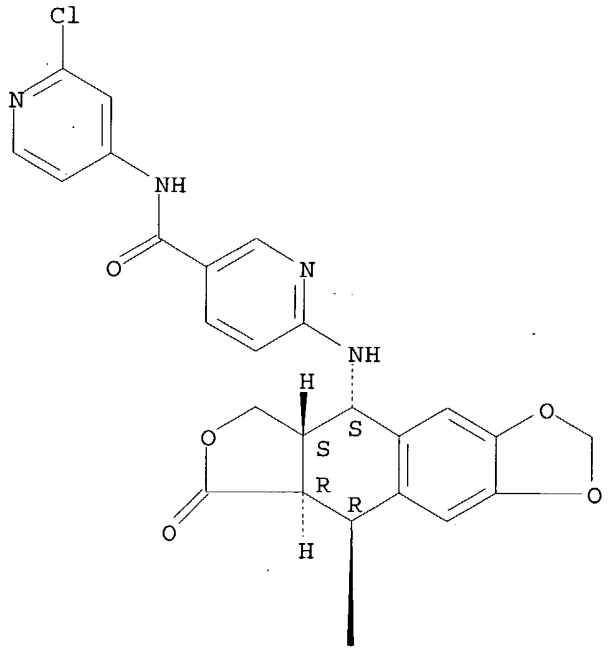

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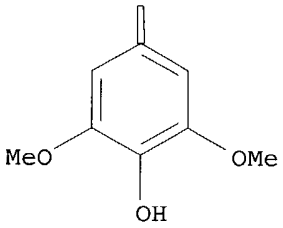
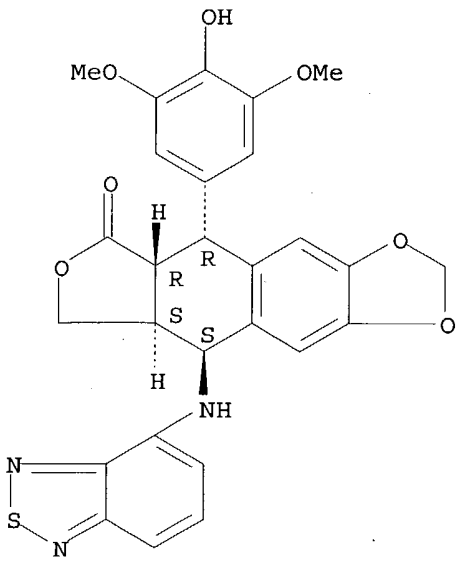


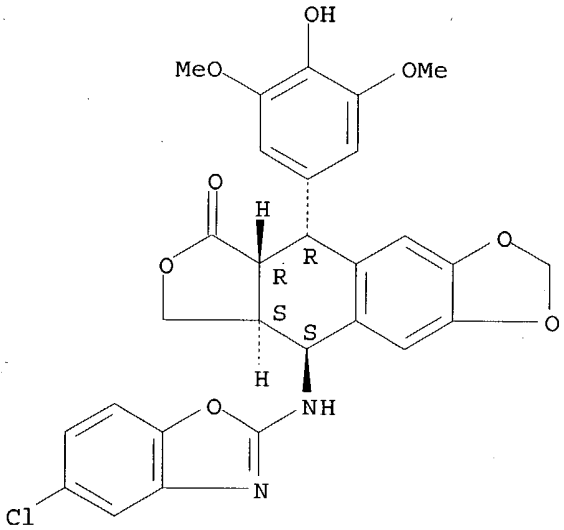
RN 681138-36-3 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-(2,1,3-benzothiadiazol-4-ylamino)-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



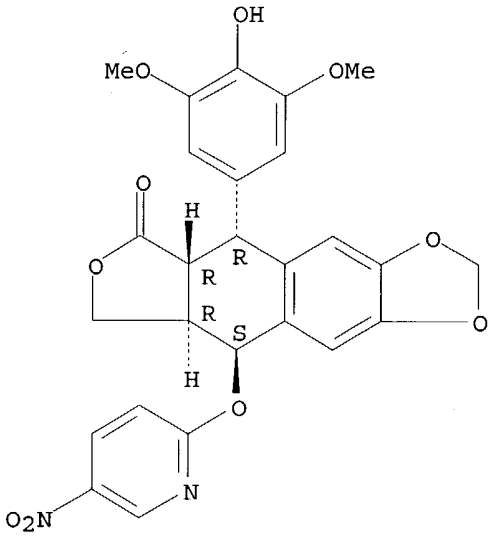
RN 681138-37-4 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[(5-chloro-2-benzoxazolyl)amino]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



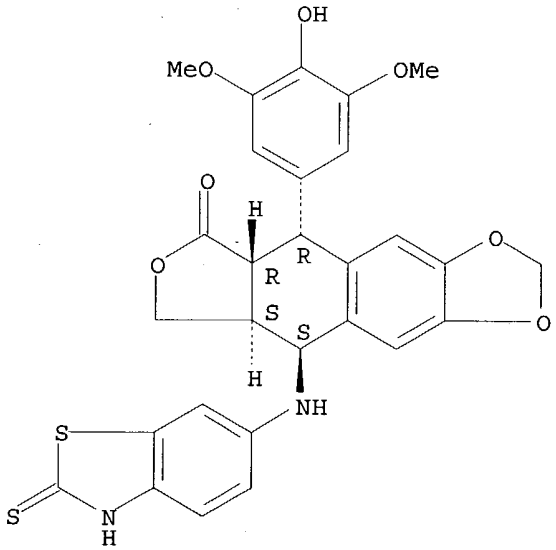
RN 681138-38-5 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(5-nitro-2-pyridinyl)oxy]-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



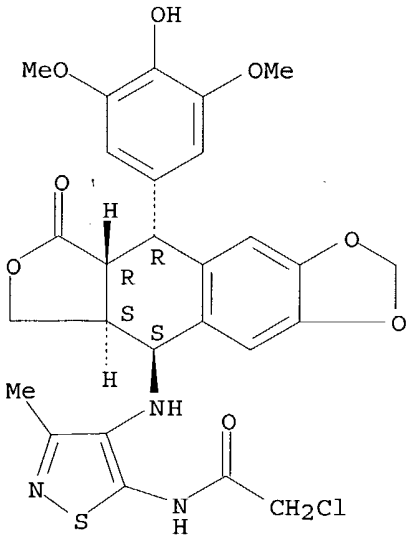
RN 681138-39-6 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[(2,3-dihydro-2-thioxo-6-benzothiazolyl)amino]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



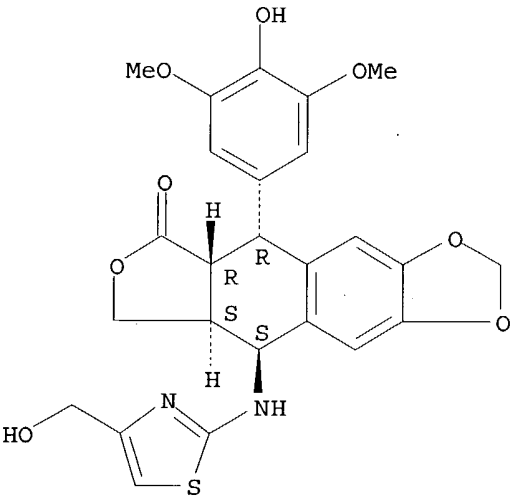
RN 681138-40-9 CAPLUS
CN Acetamide, 2-chloro-N-[4-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-3-methyl-5-isothiazolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



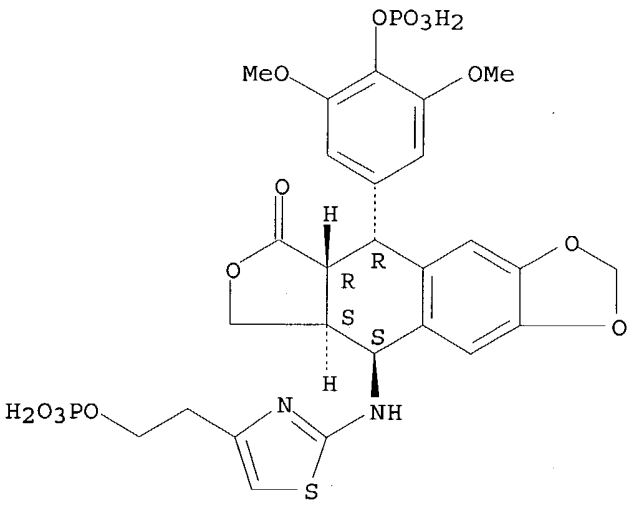
RN 681138-41-0 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[4-(hydroxymethyl)-2-thiazolyl]amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



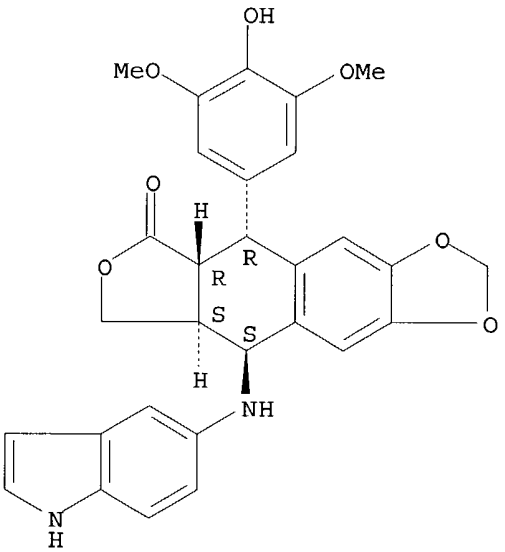
RN 681138-42-1 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5-[3,5-dimethoxy-4-(phosphonooxy)phenyl]-5,8,8a,9-tetrahydro-9-[[4-[2-(phosphonooxy)ethyl]-2-thiazolyl]amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



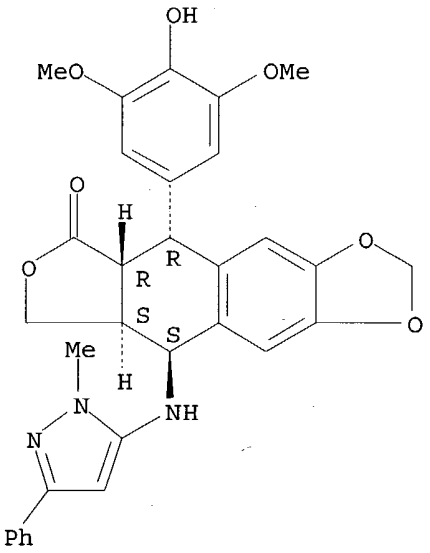
RN 681138-43-2 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-(1H-indol-5-ylamino)-, (5R,5aR,8aS,9S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



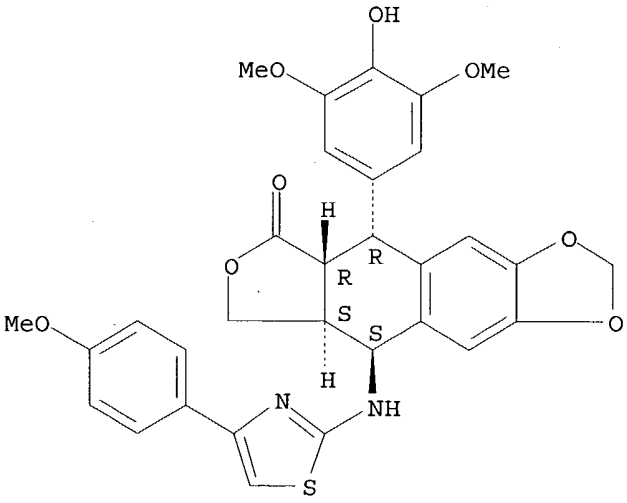
RN 681138-44-3 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(1-methyl-3-phenyl-1H-pyrazol-5-yl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



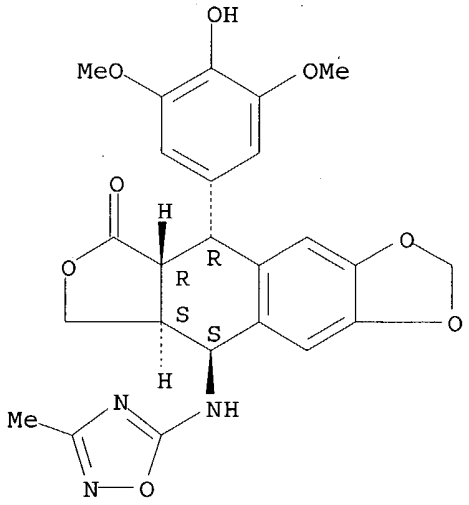
RN 681138-45-4 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[4-(4-methoxyphenyl)-2-thiazolyl]amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



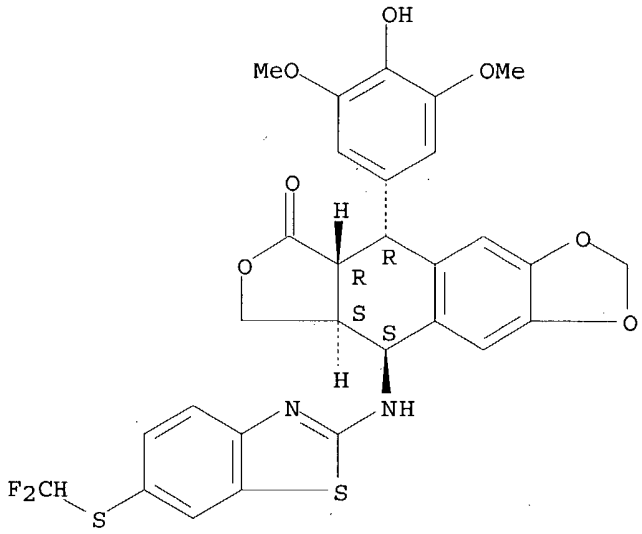
RN 681138-46-5 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(3-methyl-1,2,4-oxadiazol-5-yl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



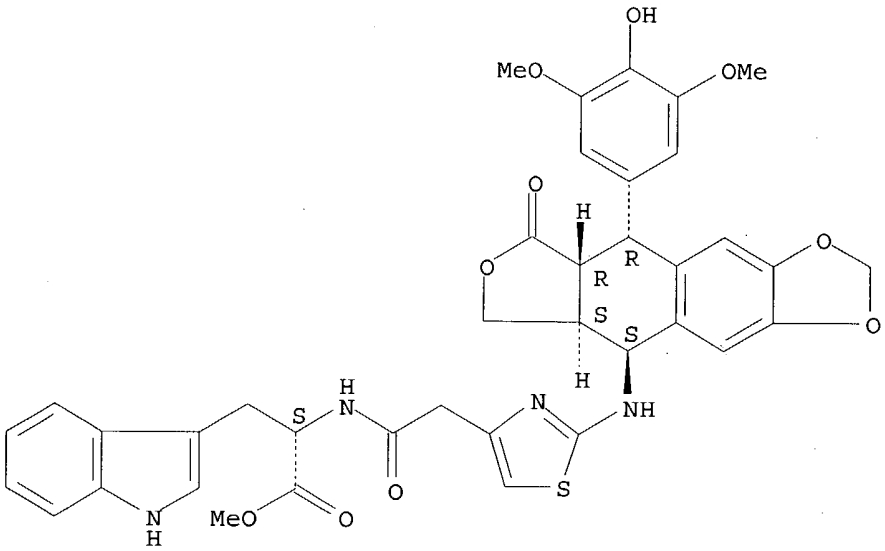
RN 681138-47-6 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[[6-[(difluoromethyl)thio]-2-benzothiazolyl]amino]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



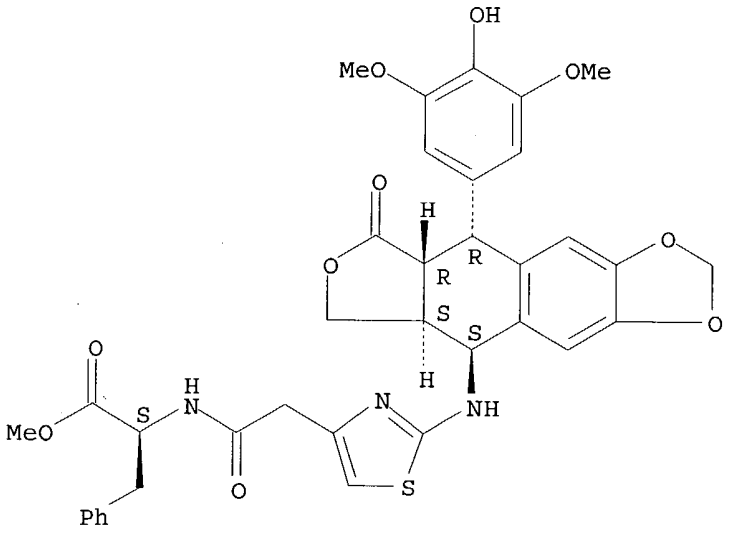
IT **681138-01-2 681138-03-4 681138-05-6**
681138-12-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of **podophyllotoxin** derivs. as anticancer compds.)
RN 681138-01-2 CAPLUS
CN L-Tryptophan, N-[[2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-4-thiazolyl]acetyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



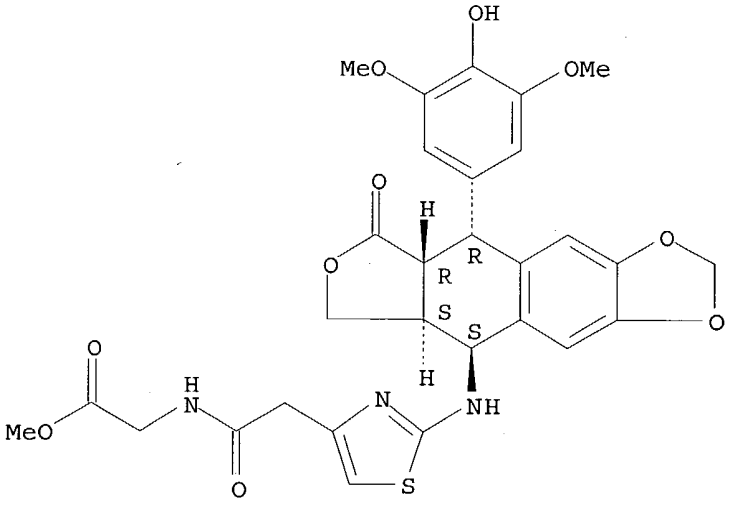
RN 681138-03-4 CAPLUS
CN L-Phenylalanine, N-[[2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-4-thiazolyl]acetyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



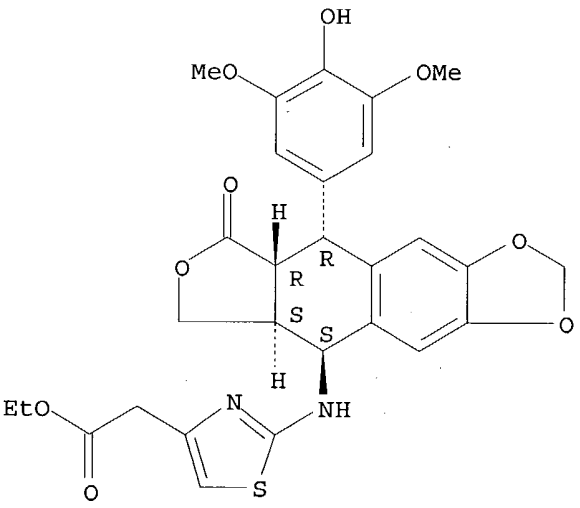
RN 681138-05-6 CAPLUS
CN Glycine, N-[[2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-4-thiazolyl]acetyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



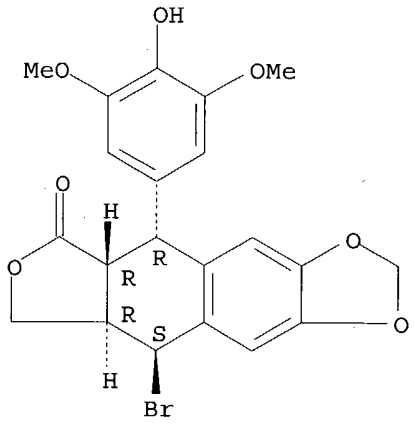
RN 681138-12-5 CAPLUS
CN 4-Thiazoleacetic acid, 2-[[(5S,5aS,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

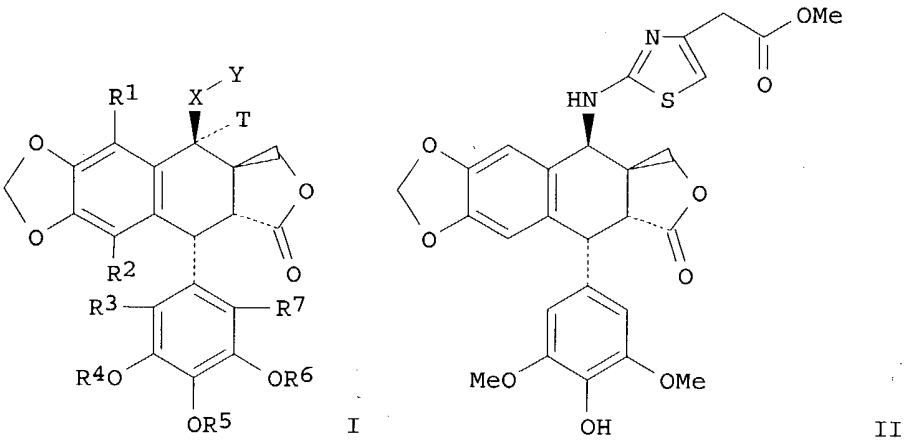


IT **16477-16-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **podophyllotoxin** derivs. as anticancer compds.)
RN 16477-16-0 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-bromo-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



GI



I II

AB **Podophyllotoxin** derivs., such as I [R1, R2, R3, R7 = H, alkyl; R4, R6 = alkyl; R5 = H, P(O)(ORa)2; Ra = H, alkyl; T = H; XT = :N; X = bond, O, S, NRb; Rb = H, alkyl; Y = 5-membered heteroaryl or heterocyclyl, optionally substituted with one or more halogen, alkyl, cyclyl, aryl, heteroaryl, heterocyclyl, etc.], were prepared for their therapeutic use as anticancer agents. Thus, **podophyllotoxin** derivative II was prepared via a multistep synthetic sequence starting from 4'-demethyl-4β-bromo-4-**desoxypodophyllotoxin** (prepared from **podophyllotoxin**), 2-aminothiazole-4-acetic acid and (trimethylsilyl)diazomethane. II showed unexpectedly high levels of cellular protein-linked DNA breaks (PLDB) induction in KB cells when tested at 5μg/mL. This invention also features a method for treating **cancer.**

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:244282 CAPLUS
DOCUMENT NUMBER: 133:53317
TITLE: Characterization of human lung **cancer** cells resistant to 4'-O-demethyl-4β-(2"-nitro-4"-

fluoroanilino)-4-**desoxypodophyllotoxin**, a unique compound in the epipodophyllotoxin antitumor class

AUTHOR(S): Tachibana, Yoko; Zhu, Xiao-Kang; Krishnan, Preethi; Lee, Kuo-Hsiung; Bastow, Kenneth F.

CORPORATE SOURCE: Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA

SOURCE: Anti-Cancer Drugs (2000), 11(1), 19-28
CODEN: ANTDEV; ISSN: 0959-4973

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

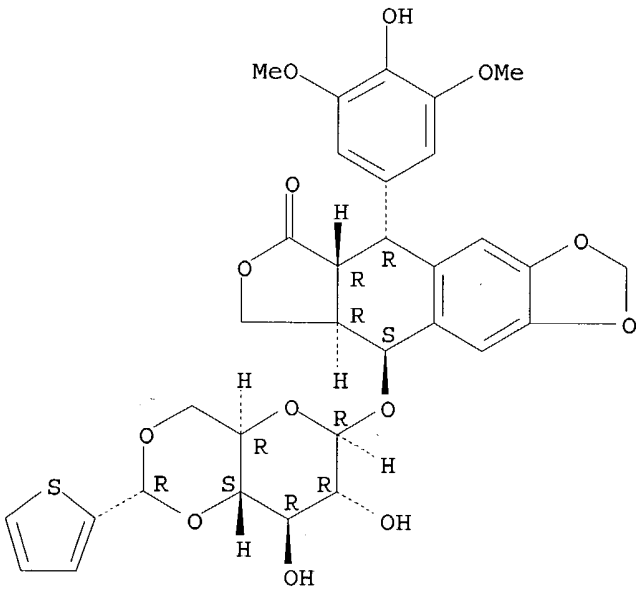
LANGUAGE: English

IT **29767-20-2**, Teniposide **33419-42-0**, VP-16 **127882-73-9**, GL-331 **276867-26-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of human lung **cancer** cells resistant to 4'-O-demethyl-4β-(2"-nitro-4"-fluoroanilino)-4-**desoxypodophyllotoxin**)

RN 29767-20-2 CAPLUS

CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[4,6-O-[(R)-2-thienylmethylene]-β-D-glucopyranosyl]oxy]-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

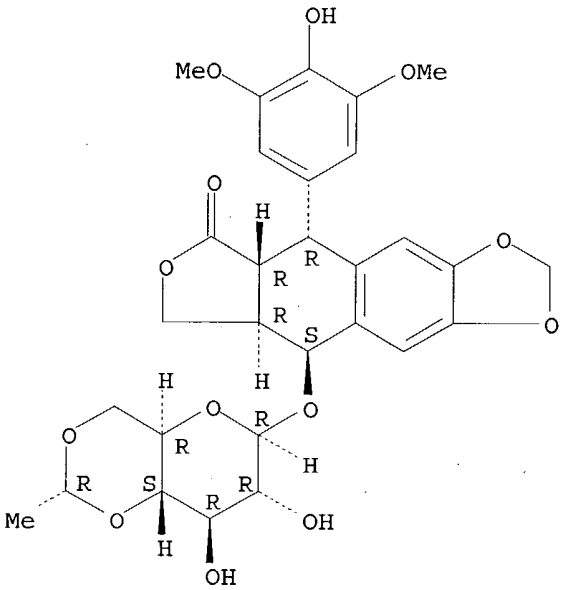
Absolute stereochemistry. Rotation (-).



RN 33419-42-0 CAPLUS

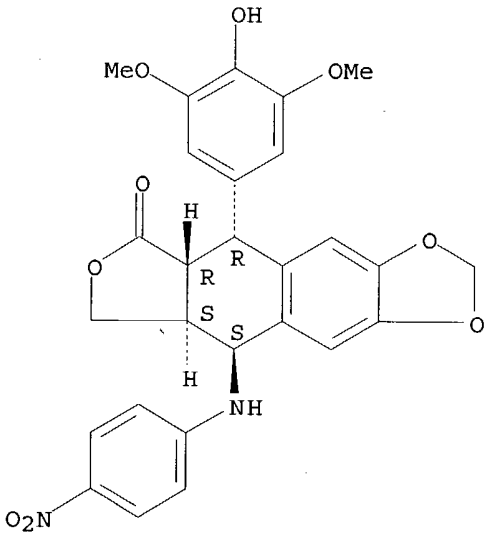
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[[4,6-O-(1R)-ethylidene-β-D-glucopyranosyl]oxy]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



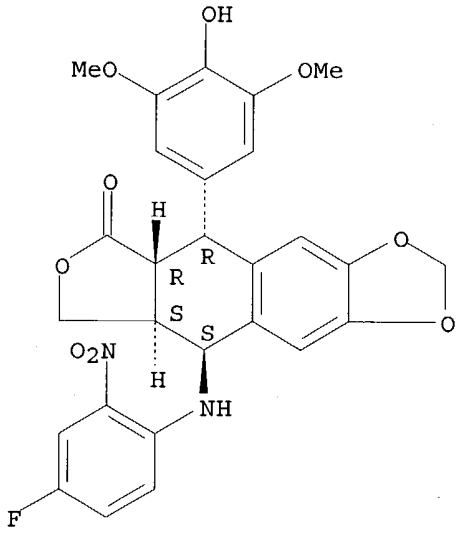
RN 127882-73-9 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[(4-nitrophenyl)amino]-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

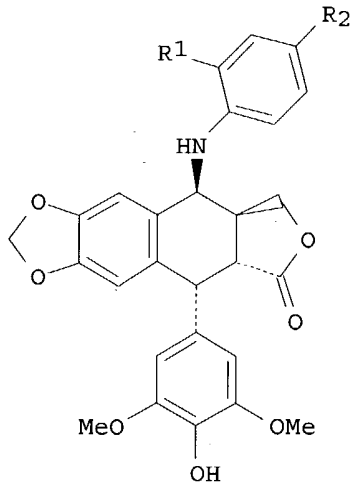


RN 276867-26-6 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[(4-fluoro-2-nitrophenyl)amino]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aS,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



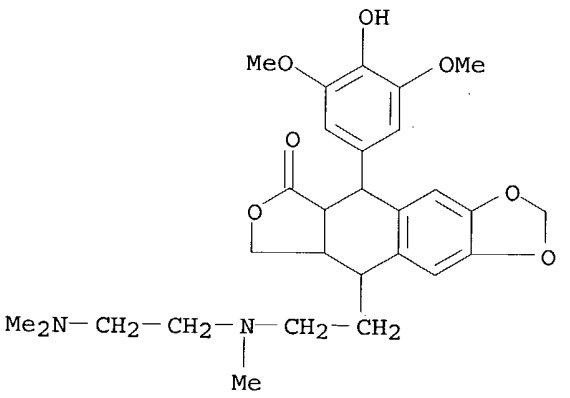
I

AB A new semi-synthetic **podophyllotoxin** derivative, 4'-O-demethyl-4β-(2"-nitro-4"-fluoroanilino)-4-**desoxypodophyllotoxin** (compound 1, I, R1= NO2, R2= F), an analog of GL-331 (compound 2, I, R1= H, R2= NO2), is a potent and broad-spectrum inhibitor of cultured human **cancer** and drug-resistant cell growth. In general, 4'-demethylepipodophyllotoxin analogs, including 2, exert anti-tumor activity by targeting the nuclear enzyme DNA topoisomerase II, but 1 is not an enzyme inhibitor. Unlike the cytotoxic activity of compound 2, cell killing by 1 is dose-limiting and a significant fraction of cells (30-40%) survive treatment. As an approach to investigate mechanism of action, 1-resistant A549 (human lung **cancer**) sub-lines were selected and characterized. Results of the work show that 1-resistant cells: (i) are moderately cross-resistant (2- to 3-fold) to various cytotoxic drugs via a P-glycoprotein-independent

mechanism, (ii) have an altered growth habit, (iii) are deficient in normal attachment on plastic and collagen substrata, and (iv) have an altered plasma membrane protein composition including several proteins in the 140->200 kDa mol. mass range and a doublet of phosphoserine-containing proteins of about 135 kDa. Since 1 treatment of cells affects neither cellular attachment or membrane-protein phosphorylation, the changes observed in 1-resistant cells are interpreted as a survival response to drug action.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:355809 CAPLUS
DOCUMENT NUMBER: 125:48601
TITLE: Antitumor activity of a novel **podophyllotoxin** derivative (TOP-53) against lung **cancer** and lung metastatic **cancer**
AUTHOR(S): Utsugi, Teruhiro; Shibata, Hiro; Kumio, Sugimoto; Aoyagi, Kumio; Wierzba, Konstanty; Kobunai, Takashi; Terada, Tadafumi; Oh-hara, Tomoko; Tsuruo, Takashi; Yamada, Yuji
CORPORATE SOURCE: Hanno Res. Center, Taiho Pharmaceutical Co., Ltd., Saitama, 357, Japan
SOURCE: Cancer Research (1996), 56(12), 2809-2814
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **148262-19-5**, TOP 53
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of a novel **podophyllotoxin** derivative (TOP-53) against lung **cancer** and lung metastatic **cancer** in relation to topoisomerase II inhibition and DNA strand breaks)
RN 148262-19-5 CAPLUS
CN Furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one, 9-[2-[[2-(dimethylamino)ethyl]methylamino]ethyl]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-, (5R,5aR,8aR,9S)- (9CI) (CA INDEX NAME)



AB We synthesized a potent new antitumor **podophyllotoxin** derivative (4β-aminoalkyl-4'-O-demethyl-4- **desoxypodophyllotoxin**;

TOP-53) in our search for a drug that has strong activity against lung **cancer** and lung metastatic **cancer.** TOP-53 exhibited twice the inhibitory activity of etoposide (VP-16) against topoisomerase II and induced DNA strand breaks but showed no inhibitory activity against tubulin polymerization The in vitro cytotoxic activity of TOP-53 assessed as IC50 was 0.016-0.37 ug/mL and 0.26-8.9 μg/mL against murine tumor and human non-small cell lung **cancer** (NSCLC) cell lines, resp. TOP-53 exerted significant efficacy equivalent to that of VP-15 on s.c.-implanted murine solid tumors (Colon 26, B16-BL6, and Lewis lung carcinoma) doses 3-5 times lower than that of VP-16. In human tumor xenografts using NSCLC, TOP-53 was active for four of five tumors, whereas VP-15 was active for two of five tumors. Potent inhibitory activity of TOP-53 was also found against a lung tumor (Lewis lung carcinoma) and four lung metastatic tumors (NL-22 and NL-17 colon **cancer**, UV2237M fibrosarcoma, and K1735M2 melanoma). TOP-53 appeared to be more active against four of them than VP-16. Thus, TOP-53 is not only active against s.c. implanted lung **cancers** but also strongly active against lung localized tumor and metastatic tumors in the lungs. The high selectivity of TOP-53 was attributed to its high distribution into the lung and its persistence. TOP-53 is expected to be highly effective against lung **cancer** including NSCLC and various lung metastatic tumors in the clin. field.

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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